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**APPLICATION NUMBER: 60/563,566**

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**PROVISIONAL APPLICATION FOR PATENT COVER SHEET**

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

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INVENTOR(S)					
Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)			
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<i>Additional inventors are being named on the _____ separately numbered sheets attached hereto</i>					
TITLE OF THE INVENTION (500 characters max)					
Transdermal Delivery of L-Arginine for the Purpose of Enhancing the Appearance of the Female Breast					
Direct all correspondence to: <b>CORRESPONDENCE ADDRESS</b>					
<input type="checkbox"/> Customer Number: <span style="border: 1px solid black; display: inline-block; width: 250px; height: 30px; vertical-align: middle;"></span>					
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<input checked="" type="checkbox"/> Firm or Individual Name <span style="border: 1px solid black; display: inline-block; width: 150px; height: 1.2em; vertical-align: middle;"></span> Eric Thor Fossel					
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ENCLOSED APPLICATION PARTS (check all that apply)					
<input checked="" type="checkbox"/> Specification Number of Pages <span style="border: 1px solid black; display: inline-block; width: 100px; height: 1.2em; vertical-align: middle;"></span> 13					
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Respectfully submitted,

SIGNATURE

TYPED or PRINTED NAME Eric Thor Fossel

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(Page 1 of 2)

Date April 19, 2004

REGISTRATION NO.

(if appropriate)

Docket Number:

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**Transdermal Delivery of L-Arginine for the Purpose of Enhancing the Appearance  
of the Female Breast**

U.S. Patent Application of:  
Eric Thor Fossel.

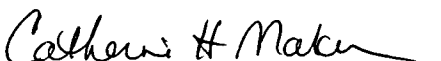
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**Related Applications**

This is a continuation in part of Serial No. 08/932,227, filed on September 17, 1997 which is herein incorporated by reference which is related to US Patent No. 5,895,658 and US Patent No. 5,922,332 and US Patent No. 6,207,714 all of which are herein incorporated by reference.

**Background****Field of the Invention**

This invention relates to improvement of the female breast size, shape and appearance through the topical application of beneficial lotions or creams.

**Prior Art**

There have been many approaches to improving the size, shape and appearance of the female breast and consist of both systemic and topical approaches. One method of tightening skin to improve appearance is through the use of cosmetic surgery. The problems associated with this approach are obvious with the high cost and the risks associated with undergoing any medically unnecessary surgery. Radiofrequency energy is one method increasingly being used to tighten skin without the need for cutting as in a conventional facelift reducing some of the potential surgical risks such as infection and anesthesia. This medical procedure is still troublesome to many individuals because it can cause damage to underlying tissues if not performed correctly.

The prior art treatment of skin without the use of cosmetic surgery involves many

different treatments but there are relatively few treatments that are actually effective in providing any noticeable benefits relative to the costs. Breast implants are effective, but are very costly and have associated health risks. Sagging breasts have also been treated surgically.

The instant invention addresses treatment of female breast to improve their size, shape and appearance without resorting to the risks and expense of surgery. Furthermore the instant invention is effective while addressing and overcoming the negative side effects of other known prior art topical skin treatments.

### **Summary of the Invention**

Accordingly, several objects and advantages of the instant invention are improve the size, shape and appearance of the female breast.

It is still another object of the instant invention to raise sagging breasts by means of enhancement of the body's own natural mechanisms.

These and other objects and features of the present invention will become apparent to those skilled in the art from reading the description of the invention, which follows.

Other objects and advantages of the present invention will become apparent from the following descriptions, taken in connection with the accompanying drawings, wherein, by way of illustration and example, an embodiment of the present invention is disclosed.

The invention provides beneficial cosmetic effects in the size, shape and appearance of the female breast by application of a cream or liquid containing a sufficient concentration of L-arginine or its derivatives to produce the desired cosmetic

effects. The cream improves the appearance of the female breast by increasing volume, resulting in increased size and significantly reducing sag.

In one embodiment of the invention, a penetrating cream containing L-arginine or its derivatives, at an effective concentration along with other substances to create a hostile biophysical environment for absorption of L-arginine into the skin is provided to produce cosmetic and structural benefits to the female breast. In this embodiment an agent or agents is combined with a sufficient concentration of L-arginine in the penetrating cream to create the hostile biophysical environment. When L-arginine is combined with a sufficient quantity of agent or agents in a penetrating cream an effective concentration of L-arginine is at least 0.1% w/v.

It was discovered that topical application of a nitric oxide precursor, L-arginine, in its various forms contained in a variety of topical preparations, either by themselves or with other agents to aid in penetration, such as a high ionic strength environment, neutralization of its charge in a complex or by other means, or included in a liposome or other biological carrier, when administered to the skin causes a beneficial cosmetic effect to the female breast.

When applied to breasts in sufficient quantity, within a short period after application with the effect lasting several hours. Further repetitive daily treatments increase the duration of the beneficial effects on appearance after application with the benefits lasting up to a period of twenty hours. The concentration of L-arginine or its derivatives can be reduced to maintain the same desired duration of cosmetic effect.

In another embodiment, the delivery vehicle is a penetrating cream, the L-arginine is present as L-arginine hydrochloride in a concentration sufficient to produce the desired effect and the penetration agents that creates the hostile biophysical

environment are ionic salts which is selected from the group consisting of sodium chloride, magnesium chloride, calcium chloride, choline chloride or combinations thereof at a concentration sufficient to aid in tissue absorption of the L-arginine.

### **Detailed Description**

Detailed descriptions of the preferred embodiment are provided herein. It is to be understood, however, that the present invention may be embodied in various forms. Therefore, specific details disclosed herein are not to be interpreted as limiting, but rather as a basis for the claims and as a representative basis for teaching one skilled in the art to employ the present invention in virtually any appropriately detailed system, structure or manner.

The invention consists of a base cream or liquid with the properties of excellent absorption into the skin that contains a concentration of at least 0.1%, preferably at least 10% of L-Arginine alone or in conjunction with the adjunct theophylline to the female breast resulting in improved appearance size and shape including a reduction of sag.

In another embodiment the cream contains L-arginine or its derivatives, and it is combined with agents that aids penetration. The effective range of L-arginine or it's derivatives is about 0.1 to 25% w/v alone or with the adjunct theophylline when used in conjunction with an effective concentration of penetrant aid. The concentration of L-arginine alone or with the adjunct theophylline in the cream can be reduced with the inclusion of a greater amount or concentration of penetration aids or increased to lengthen the beneficial cosmetic effect. The concentration of L-arginine alone or with the adjunct theophylline when combined with an effective penetration aid is preferably at least about 5% w/v or greater.



In one embodiment the cream contains the L-arginine the derivative of L-arginine hydrochloride with at least 12.5% w/v, either by itself or in conjunction with the adjunct theophylline (10% w/v) and is combined with choline chloride having at least 10% weight by volume, sodium chloride with at least 5% weight by volume, and magnesium chloride with at least 5% weight by volume. The optional additional components of the base cream may be water, mineral oil, glyceryl stearate, squalene, propylene glycol stearate, wheat germ oil, glyceryl stearate, isopropyl myristate, steryl stearate, polysorbate 60, propylene glycol, oleic acid, tocopherol acetate, collagen, sorbitan stearate, vitamin A & D, triethanolamine, methylparaben, aloe vera extract, imidazolidinyl urea, propylparaben, and BHA or any combination thereof.

L-arginine hydrochloride provides a precursor to the molecule, nitric oxide, NO. Nitric oxide is the substance that relaxes the blood vessels, allowing for increased blood flow. Choline chloride, sodium chloride and magnesium chloride provides a high ionic strength environment for the highly charged molecule, L-arginine. This high ionic strength environment is an example of a hostile biophysical environment for L-arginine. That is, the highly charged ionic strength is an unfavorable environment for the highly charged L-arginine making the L-arginine anxious to move to a more hospitable, less charged environment such as human tissue. The base cream containing L-arginine, choline chloride, sodium chloride and magnesium chloride is the agent that produces beneficial effects such as improvement of the appearance, size and shape and reduction of sag in the female breast.

#### **Other Embodiments -Other active agents**

While L-arginine hydrochloride is the preferred active agent because it is the agent in

nature itself, it is non-toxic, is highly soluble and it is inexpensive, other agents could be used which are also precursors or donors of nitric oxide. These include D,L -arginine, L-arginine, alkyl (ethyl, methyl, propyl, isopropyl, butyl, isobutyl, t- butyl) esters of L-arginine and salts thereof as well as other derivatives of arginine and other nitric oxide donors. Pharmaceutically acceptable salts include hydrochloride, glutamate, butyrate, and glycolate.

In the case of an alternative active agent were used it would be simply substituted for L-arginine in a delivery preparation and the preparation used as in the case of the L-arginine preparation.

### **Other Means of Effecting or Improving Absorption**

A variety of means for effecting or improving absorption of the active agent can be envisioned. One principle behind the absorption of a highly charged molecule such as L-arginine into tissue is to either create a biophysically hostile environment in the delivery vehicle such that L-arginine would prefer to be in tissue, or to package L-arginine in such a way that it is carried into tissue or neutralize its charge by derivitization or forming a neutral salt. Examples of biophysically hostile environments, include but are not limited to; high ionic strength by the addition of ionic salts such as sodium chloride, magnesium chloride or choline chloride; high or low pH by adding pharmaceutically acceptable acids or bases; and highly hydrophobic environments by decreasing water content and increasing lipid, oil and/or wax content. Examples of packaging which would be carried into tissue includes liposomes or emulsions of collagen, collagen peptides or other components of skin or basement membrane. Examples of neutralization of charge include delivery of the active agent in the form or

an ester or salt such as arginine glutamate, which is electronically neutral.

In each case of creating a hostile biophysical environment for the active agent, the agent was added to an appropriate preparation. In the case of creating a high ionic strength ions such as but not limited to sodium chloride, potassium chloride, choline chloride, magnesium chloride, lithium chloride, alone or in combination were added in high concentration. Other highly charged molecules such as polylysine, polyglutamine, polyaspartate or copolymers of such charged amino acids may be used to create the hostile biophysical environment.

Alternatively a hostile biophysical environment may be created by placing the highly charged L-arginine in an hydrophobic, oily environment such as in an oil-based cream containing little or no water. Absorption may further be aided by combining the use of hostile biophysical environments with the use of penetrating agents such as oleoresin capsicum or its constituents or molecules containing heterocyclic rings to which are attached hydrocarbon chains.

### **Reduction of breast sagging and increase of breast firmness**

#### **Example 1**

In this example a 60-year-old woman with pendulous breasts was provided with a penetrating cream comprising L-arginine (12.5% w/v), sodium chloride (10% w/v) and magnesium chloride (5% w/v). The cream was applied to one of the breasts, which was rubbed in extensively for maximal absorption. After a period of approximately 20 minutes the treated breast was much fuller and raised up by about 1.5 inches. The effect of the initial treatment lasted for a period of about seven hours.

The concentration of L-arginine can be reduced to decrease the duration of the

cosmetic effect of the initial application. The minimum effective concentration of L-arginine or its derivatives is about at least 0.5% w/v, but it is preferably a greater initial treatment amount otherwise the initial duration of the cosmetic benefit will be too brief. The concentration of L-arginine is tailored to have a duration of at least 3 hours, preferably 8 or more. This is dependent upon the concentration of penetration aid used in conjunction with the L-arginine. The concentration to produce a beneficial cosmetic effect during initial application, of at least 3 hours, is at least 5%.

## **Example 2**

In this example a 47-year-old woman with extremely pendulous breasts applied a breast lifting cream comprising L-arginine (12.5% w/v), choline chloride (10% w/v), sodium chloride (10% w/v) and magnesium chloride (5% w/v). The breast lifting creaming was rubbed vigorously into each breast for about five minutes. Within one hour both breasts were noticeably firmer and had been lifted about 2.75 inches. The effect of the initial treatment lasted for about five hours.

The treatment was continued daily for about a month. The lifting effect of the treatment had an effective duration of about eighteen to twenty hours after a month of daily use.

The concentration of L-arginine can be maintained to continue cosmetic benefits for up to twenty hours if the same cream is applied on a regular basis of once every 8 to 48 hours, preferably every 12-36 hours.

## **Claims**

What is claimed is:

1. A method of delivering a nitric oxide releasing substance selected from the group consisting of L-arginine, L-arginine salts and L-arginine derivatives in a cream which is applied to the breasts of women for the purpose of improving breast size, shape and appearance and to reduce sag resulting in delivery effective amount of L-Arginine, its salts or its derivatives and wherein said vehicle creates a hostile biophysical environment for the substance which causes the substance to migrate from the vehicle across the skin into the tissue of the breast.
2. The method of claim 1 where the vehicle containing the hostile biophysical environment has a pH between 3 and 11.
3. The method of claim 1 where the hostile biophysical environment is created by high concentrations of ionic salts such as sodium chloride, choline chloride, magnesium chloride, calcium chloride and other ionic salts of that class.
4. The method of claim 1 where the ionic strength is 0.25 molar to 15 molar and is created by adding salts such as sodium chloride, potassium chloride, choline chloride, magnesium chloride, calcium chloride and others of this class.
5. The method of claim 1 where concentration of L-Arginine is 0.05-25% w/v

6. The method of claim 1 where the cream is comprised of all or some of the following: Water (20-80%), white oil (3-18%), glyceryl stearate (0.25-12%) squalene (0.25-12%), cetyl alcohol (0.1-11%), propylene glycol stearate (0.1-11%), wheat germ oil (0.1-6%), polysorbate 60 (0.1-5%), propylene glycol (0/05-5%), collagen (0.05-5%), sorbitan stearate (0/05-5%) vitamin A&D (0/02-4%), vitamin E (0.02-4%), triethanolamine (0.01-4%), methylparaben (0.01-4%), aloe vera extract (0/01-4%), imidazolidinyl urea (0.01-4%) propylparben (0.01-4%), bha 0.01-4%), L-Arginine Hydrochloride (0.25-25%), sodium chloride (0.25-25%), magnesium chloride (0.25-25%) and choline chloride (0.25-25% w/v) and the pH is between 3 and 11.

7. A method of delivering a nitric oxide releasing substance selected from the group consisting of L-arginine, L-arginine salts and L-arginine derivatives and adjuncts such as theophylline to the breasts of women desiring an improvement of size, shape and appearance and reduction of sag of the breasts applying to the breasts a cream containing an effective amount of L-Arginine, its salts or its derivatives and wherein said vehicle creates a hostile biophysical environment for the L-Arginine and theophylline which causes the substances to migrate from the vehicle across the skin into the tissue.

8. The method of claim 7 where the vehicle containing the hostile biophysical environment has a pH between 3 and 11.

9. The method of claim 7 where the hostile biophysical environment is created by high concentrations of ionic salts such as sodium chloride, choline chloride, magnesium chloride, calcium chloride and other ionic salts of that class.

10. The method of claim 7 where the ionic strength is 0.25 molar to 15 molar and is created by adding salts such as sodium chloride, potassium chloride, choline chloride, magnesium chloride, calcium chloride and others of this class.

11. The method of claim 7 where concentration of L-Arginine is 0.05-25% ( w/v) and theophylline is 0.05-25% (w/v).

12. The method of claim 7 where the cream is comprised of some or all of the following: Water (20-80%), white oil (3-18%), glyceryl stearate (0.25-12%) squalene (0.25-12%), cetyl alcohol (0.1-11%), propylene glycol stearate (0.1-11%), wheat germ oil (0.1-6%), polysorbate 60 (0.1-5%), propylene glycol (0/05-5%), collagen (0.05-5%), sorbitan stearate (0/05-5%) vitamin A&D (0/02-4%), vitamin E (0.02-4%), triethanolamine (0.01-4%), methylparaben (0.01-4%), aloe vera extract (0/01-4%), imidazolidinyl urea (0.01-4%) propylparben (0.01-4%), bha 0.01-4%), L-Arginine Hydrochloride (0.05-25%), theophylline (0.05-25%) sodium chloride (0.25-25%), magnesium chloride (0.25-25%) and choline chloride (0.25-25% w/v) and the pH is between 3 and 11.

**Abstract**

The present invention provides a improvement of the size, shape, and appearance and reduction of sag of female breasts. A topical cream is described which improves blood flow by the transdermal delivery of the nitric oxide precursor L-Arginine either alone or with an adjunct, theophylline. The delivery of the active agents is accomplished by use of a vehicle which contains a hostile biophysical environment which is also hostile to hydrogen bond formation.